with the *ureH* sequence or with a sequence that is complementary to the *ureH* sequence and not to other sequences in *H. pylori*.

67. The purified polypeptide according to claim 62, having an amino acid sequence encoded by a purified nucleic acid sequence comprising the *ureI* gene represented by nucleotides 211 to 795 of SEQ ID NO:1 and Figure 4 or a sequence comprising at least 20 contiguous nucleic acid residues that hybridizes under stringent conditions selected from the group consisting of

a) 68°C in 6 x SSC Denhardt medium; and

b) 37°C in 5 x SSC 50% formamide

with the *ureI* sequence or with a sequence that is complementary to the *ureI* sequence and not to other sequences in *H. pylori*. --

REMARKS

Applicants respectfully draw the Examiner's attention to the Revocation of Original Power of Attorney and Grant of New Power of Attorney filed by the assignee on June 19, 1997, naming the firm of Finnegan, Henderson, Farabow, Garrett, & Dunner, L.L.P. as attorneys of record. The new Attorney Docket No. is 02356.0074-00000. If there is some reason that this Revocation and new Power has not been entered, applicants request that the Examiner notify the undersigned attorney.

Applicants have deleted claims 1-17 and 20-36 directed to non-elected subject matter. Applicants have deleted claims 46-51 and added claims 62-67 directed to the same subject matter. Claims 62-67 mirror the language allowed in divisional application Serial No. 08/472,285. Claims 62-67 are fully supported by the application as filed (e.g., at pages 14, 16,

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18, and at Figure 9) and by canceled claims 46-51. Claims 40-45 and 52-67 are now pending in this application.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 40-61 under 35 U.S.C. § 112, second paragraph, as allegedly vague due to improper Markush format. Applicants have amended the claims to overcome this rejection.

The Examiner has rejected claims 53-58 as allegedly vague and indefinite because the claims do not clearly recite "monoclonal" or "polyclonal" antibodies. Applicants disagree that claims 53-58 are indefinite. The term "antibodies" is intended to include both polyclonal and monoclonal antibodies. The specification identifies both monoclonal and polyclonal antibodies as falling within the scope of the invention (page 18, lines 33-36). Applicants respectfully submit that the skilled artisan would understand that the claims cover both monoclonal and polyclonal antibodies. Recitation of one or both of these terms is not necessary to apprise the person of ordinary skill in the art of the scope of the claims. Accordingly, amendment of claims 53-58 is not necessary to comply with 35 U.S.C., second paragraph, and applicants request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner objected to the specification and rejected claims 40-61 under 35 U.S.C. § 112, first paragraph. The Examiner contends that the specification does not enable one of skill in the art to use the claimed invention because "it is unclear how the products, polypeptides from these genes can be used in compositions to treat infection due to *H. pylori*." The Examiner relies on a 1992 article by Cussac et al. which states that, with the exception of UreA and UreB, "no

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role can as yet be assigned to the nine proteins encoded by the *H. pylori* urease gene cluster." Applicants traverse.

Applicants' specification teaches that the presence of the five urease accessory genes is essential to the expression of functional urease (page 14, lines 20-23), i.e., the claimed polypeptides have been implicated particularly in the regulation and the maturation of the urease in *H. pylori* (page 18, lines 27-29). The specification also teaches that the polypeptides of the invention can be used for the production of monoclonal or polyclonal antibodies, or for the detection of antibodies in a biological sample infected by *H. pylori* (page 18, lines 36). In addition, one of skill in the art would clearly recognize that the antibodies themselves may be used to detect the presence of native polypeptides in a biological sample infected by *H. pylori*.

Based on these teachings, one of skill in the art would understand how, i.e., be enabled, to use the claimed polypeptides to raise antibodies, which in turn may be used to detect *H. pylori* in a properly prepared biological sample. The single, isolated statement from Cussac et al., cited by the Examiner, does not undermine the teachings in the application. Indeed, a proper reading of the statement suggests that the authors were referring to the biological role of the polypeptides in the life cycle of *H. pylori*, not to the utility of the polypeptides in the diagnosis and treatment of *H. pylori* infections. In fact, the article taken as a whole supports the teaching of the application.

The PTO has the burden of establishing a *prima facie* case of lack of enablement. In re Marzocchi, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). Furthermore, applicants' specification disclosing how to make and use the claimed invention must be taken as in compliance with §112, first paragraph, unless there is a reason to doubt the objective truth of the disclosure. In re Brana, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1437, 1442 (Fed. Cir. 1995). No reasons sufficient to cast

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doubt on applicants' teachings have been provided. One having ordinary skill in the art would be capable of practicing the claimed.

The Examiner contends that "the antigenic determinants or epitopes have not been disclosed for the *H. pylori* urease" and that "the specification has not taught the use of fragments; how to obtain these fragments or how much of the polypeptide constitutes a fragment." Applicants traverse. Epitope mapping is a skill well known and widely practiced in the art. The Patent Office routinely acknowledges this fact and currently concedes enablement for "immunogenic fragments" of a given sequence. In view of the fact that applicants have provided the amino acid sequences of the claimed polypeptides, the basis for the Examiner's concern is not apparent.

Applicants respectfully submit that the "fragments" of the purified polypeptides of claim 40 are enabled by the specification. For example, the passage at page 14, line 27 through page 4, line 9 specifically addresses the fragments of the claimed invention. In addition, at page 15, lines 1-5, applicants provide a simple assay to determine whether a polypeptide fragment is within the scope of the invention:

> This functional homology can be detected by implementing the following test: 10^9 bacteria are resuspended in 1 ml of urea-indole medium and incubated at 37°C. The hydrolysis of the urea leads to the release of ammonia which, by raising the pH, leads to a colour change from orange to fuchsia.

(Specification at page 15, lines 1-5). The same functional homology test can be applied to enable the polypeptides encoded by the specific nucleotide sequences recited in claims 62-67. Therefore, applicants respectfully submit that it would require only routine experimentation by one having ordinary skill in the art to determine what polypeptides and fragments are useful in

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the claimed invention and request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. §§ 102/103

Claims 40, 45, 46, 51, 59, and 60 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over Tabaqchali et al. Applicants traverse.

Tabaqchali et al. neither teaches nor suggests the claimed polypeptides. Tabaqchali et al. discloses a nucleotide and corresponding amino acid sequence for *H. pylori* urease gene subunits A and B (see Appendix, page 15). The Examiner contends that because nucleic acids 2622 to 2693 correspond to the gene known as UreI, that Tabaqchali et al. anticipates or renders obvious the claimed invention. Applicants disagree. Tabaqchali et al. does not teach that nucleic acids 2622 to 2693 encode the UreI polypeptide as claimed by applicants. In fact, Tabaqchali et al. never even identifies these nucleotides except as part of the whole sequence of 2767 nucleotides. Tabaqchali et al. does not teach or suggest the existence of any urease polypeptides other than UreA and UreB. Tabaqchali does not teach or suggest that any part of the 2767 (including signal sequence) nucleotide sequence is useful to produce a polypeptide other than UreA or UreB.

Furthermore, Tabaqchali et al. actually teaches away from applicants' invention. At pages 15-18 of the publication, Tabaqchali et al. clearly teaches that nucleotides 2622 to 2693 are non-coding and include downstream vector linking sequences. Tabaqchali does not teach or suggest that nucleotides 2622 to 2693 should be, or even could be, used to generate a distinct urease polypeptide.

It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81, 90 (Fed. Cir.

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1986), cert. denied, 480 U.S. 947 (1987). Tabaqchali et al. does not describe the purified UreI polypeptides of claims 40, 45, 46, 51, 59, or 60. Thus, Tabaqchali et al. cannot anticipate the claimed invention. Nor, in view of the clear teaching away from the applicants invention, can Tabaqchali et al. render the claims obvious. Accordingly, applicants request that the Examiner reconsider and withdraw this rejection.

Claims 40-61 are rejected under 35 U.S.C. § 102(a) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over Cussac et al. Claims 53-61 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Cussac et al. taken with Siever. Applicants traverse.

Cussac et al. is not prior art. Cussac et al. was published in April 1992, well after the October 3, 1991, priority date of the present application. Accordingly, Cussac et al. does not anticipate or render the claimed invention obvious, alone or in combination with any other document. Applicants' claim to the October 3, 1991, priority date was perfected under the Patent Cooperation Treaty, before this application entered national phase in the United States. Nothing more is required. Accordingly, applicants request that these rejections be withdrawn.

In view of the foregoing amendments and arguments, applicants respectfully submit that this application is now in condition for allowance. Reconsideration and reexamination of the application and the timely allowance of the pending claims are earnestly solicited.

Respectfully submitted,

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Dated: February 12, 1998

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